Original Article

Spontaneous bacterial peritonitis among adult patients with ascites attending Korle-Bu Teaching Hospital

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SUMMARY

Background: Spontaneous bacterial peritonitis (SBP) is one of the most common and life-threatening complications of ascites, mostly in patients with cirrhotic ascites and children with nephrotic syndrome. Recognition and prompt treatment of this condition is essential to prevent serious morbidity and mortality. It is therefore important to determine the prevalence of SBP among in-patients with ascites attending our facility and to determine the clinical characteristics associated with SBP among these patients.

Methods: A cross-sectional study was conducted involving 140 patients with ascites irrespective of the underlying cause from 25th March 2016 to 25th November 2016. Demographic information and clinical data were collected using a standardized questionnaire. Ascitic fluid culture, the gold standard for SBP diagnosis and ascitic fluid cell count was done. Positive ascitic fluid culture and/ or ascitic polymorpho nuclear leukocyte ≥250cells/mm3 were diagnostic for SBP

Results: Of the 140 patients with ascites the mean age was 44.7±13.2 years. There were seventy six (76) male and sixty four (64) female patients. The prevalence of SBP was 21.43% (30/140). Majority, (41.7%) of the bacteria isolated from ascitic fluid with SBP was Escherichia coli. History of jaundice, low arterial blood pressure on admission and encephalopathy were found to be independent predictors of SBP.

Conclusion: SBP is common among patients with ascites admitted at the Korle-Bu Teaching Hospital. Jaundice, encephalopathy and low blood pressure are highly suggestive of SBP and diagnostic paracentesis should be done immediately on admission to confirm the diagnosis.

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INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is defined as an ascitic fluid infection without an evident intra-abdominal, surgically treatable source.[1] The diagnosis is established by a positive ascitic fluid bacterial culture and an elevated ascitic fluid absolute polymorphonuclear leukocyte (PMN) count (≥250 cells/mm^3). An elevated ascitic fluid absolute PMN count (≥250 cells/mm^3) is adequate to make a presumptive diagnosis of SBP and to start empiric therapy. Spontaneous bacterial peritonitis is one of the most serious sequelae of ascites.

It is a very common bacterial infection in patients with ascites, occurring mostly in patients with cirrhosis, requiring prompt recognition and treatment. SBP was presumed to occur only in individuals with alcoholic cirrhosis. SBP is now known to affect patients with cirrhosis from any cause as well as any disease state leading to ascites such as heart failure, cancer, nephrotic syndrome, systemic lupus erythematosus and Budd-Chiari syndrome.[2,3,4,5] Ascitic fluid infection is the most frequent infectious complication among patients with cirrhosis and ascites.[6] The prevalence of SBP in the past was relatively low at 5% to 10% in cirrhotic patients with ascites.[7]

However, recent studies using newer diagnostic criteria and improved culture techniques have estimated a prevalence of 10% to 30% in cirrhotic patients with ascites admitted to hospitals and 3.5% among outpatients.[8,9,10] In-hospital mortality for the first episode of SBP ranges from 10% to 50%, depending on various risk factors.[11]

In 40%-70% of patients, SBP relapse occurs within 1 year.[12] One-year mortality after a first episode of SBP has been reported to be 31% and 93%.[13]

Independent prognostic factors include Child-Pugh grade C liver cirrhosis, renal dysfunction, elevated blood urea nitrogen level before occurrence of peritonitis, age, intensive care unit admission, positive ascitic fluid culture and elevated serum bilirubin level during infection.[13, 14]

Although the prognosis of SBP has improved in recent years with the advent of effective antibiotics and prompt intervention, the long-term prognosis of SBP remains extremely poor due to severe impairment of liver function. After an initial diagnosis of SBP, 1- month, 6-month and 1-year mortality rates are 33%, 50% and 58% respectively.[15] Liver transplantation should therefore be considered for patients who survive an episode of SBP.

The pathogenesis of SBP involves the interaction of gut microbiota, increased intestinal permeability, bacterial translocation and immune deficiency which may be acquired or conferred by genetic susceptibility. These factors act in concert as pathophysiological culprits for the development of SBP that is seen in cirrhosis. Factors associated with the risk of developing spontaneous bacterial peritonitis are upper GI bleeding, poor liver function, low ascitic fluid protein levels, prior SBP and hospitalization.[16,17] Bacteria most commonly isolated from ascitic fluid in patients with SBP are usually made up of the normal intestinal flora.[18,19] More than 92% of all cases are monomicrobial with aerobic gram negative bacilli being responsible for more than two thirds of cases.[18]

Escherichia coli (E. coli) accounts for nearly half of these cases followed by Klebsiella species and other gram negative bacteria. Twenty-five percent of cases are caused by gram positive organisms with Streptococcus species being the most common.[18] In bacterial peritonitis associated with peritoneal carcinomatosis, the microorganisms isolated are not usually known to cause SBP, and are particularly virulent, for example, Salmonella spp. SBP is rarely caused by anaerobic organisms, so their presence in ascitic fluid should raise suspicion of an alternative cause. Rarely, the bacteria may reach the ascitic fluid from the urinary or respiratory tracts.[20,21]

The symptoms and signs of spontaneous bacterial peritonitis (SBP) are subtle compared with those of patients who have surgical peritonitis in the absence of ascites. SBP may be asymptomatic in about 10-32% of cases, particularly in patients with ascites attending outpatient clinic.[22,24] Symptoms and signs at the time of diagnosis in 489 patients with spontaneous bacterial peritonitis were fever (69%), abdominal pain (59%), altered mental status (54%), abdominal tenderness (49%), diarrhoea (32%), paralytic ileus (30%), hypotension (21%) and hypothermia (17%).[25] The aim of this study was to determine the prevalence of spontaneous bacterial peritonitis among patients with ascites and to examine the clinical characteristics associated with SBP among hospital based patients. The long-term significance would be to contribute to the effective management of patients with ascites through early diagnosis, documentation and prompt treatment of SBP among these patients.

METHODS

Research design

The research design was a cross-sectional hospital-based study, carried out at the Department of Medicine, Korle-Bu Teaching Hospital (KBTH), Accra, from 1st March 2016 to 25th November 2016.

Patient Selection

One hundred and forty (140) patients with ascites admitted to the medical block were consecutively recruited. All adult patients above 18 years with ascites who provided informed consent were included. Exclusion criteria were patients who had already been started on antibiotics at the time of recruitment or who had taken antibiotics up to 2 weeks preceding recruitment, as well as refusal of consent. Diagnosis of ascites was made based on the clinical features of abdominal distension, the presence of shifting dullness and/ or positive fluid thrill. It was subsequently confirmed by diagnostic paracentesis or an abdominal ultrasound scan.

Data Collection and Measurements

Patients' medical records were reviewed to exclude those with ascites who were on antibiotics or had been on antibiotics in the preceding two weeks to the date of recruitment.

Relevant history including alcohol use and physical characteristics including clinical features of liver cirrhosis (spider angioma, palmar erythema, ascites, asterixis, hepatomegaly, splenomegaly, and abdominal vein collaterals); congestive heart failure (orthopnoea, paroxysmal nocturnal dyspnoea, bilateral crepitations increased Jugular venous pressure); nephrotic syndrome (anasarca, pleural effusion); lymphoma (weight loss, fever, anorexia, generalized lymphadenopathy); abdominal tuberculosis (ascites, weight loss, anorexia, pleural effusion); chronic kidney disease (pedal oedema, symptoms and signs of anaemia, pulmonary oedema);

and other causes of ascites were recorded. Ascites was graded as mild (detectable only on ultrasound), moderate (visible moderate symmetrical abdominal distension) or severe (marked abdominal distension).
After thoroughly explaining the study to patients, those who gave informed consent were recruited and a questionnaire was administered (socio-demographic data and clinical history of the patients were obtained). A sample of 15mls of venous blood was taken for haematological, biochemical and serological investigations.

Abdominal paracentesis was performed using an aseptic technique at the right or left iliac fossa, 3cm above and 3cm medial to the anterior superior iliac spine. Exactly 15mls of ascitic fluid was collected using a sterile syringe and 10mls inoculated into a blood culture bottle on the bed side for culture and 5mls was inoculated into a sterile ethylenediaminetetraacetate (EDTA) bottle and sent to the laboratory for cell count and differentials, albumin and protein. Furthermore, an abdominal ultrasound scan, chest x-ray and urinalysis were performed.

Blood Tests
Hematological and biochemical workup included measurement of hemoglobin (HB), white blood cell count (WBC), platelet (PLT) count, international normalized ratio (INR), and serum concentrations of total (TOT) and direct (DIR) bilirubin, protein, albumin, alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Serum sodium (Na^+), potassium (K^+), urea and creatinine testing were also performed for all patients and their estimated glomerular filtration rate calculated. Urine analysis (Proteins, leucocytes, erythrocytes, pus cell and other urine abnormalities) was done for all patients. All patients were tested for Hepatitis B surface antigen (HBsAg) and anti-bodies to hepatitis C virus (anti HCV-Ab) to determine the causes of liver cirrhosis.

Ascitic Fluid Analysis
Ascitic fluid analysis including cell count and differentials, albumin and protein was performed for all patients. Further tests done on the ascitic fluid if needed to confirm the diagnosis of the cause of ascites included adenosine deaminase, lactate dehydrogenase, serum amylase, P^H, acid fast bacilli and a cytology report. Ascitic fluid culture: 10 mls of ascitic fluid was collected during the diagnostic abdominal paracentesis and put into a blood culture bottle. Ascitic fluid culture was done by inoculating the ascitic fluid into Blood Agar and MacConckey Agar. Preliminary results were obtained after 48 hours, followed by conventional biochemical identification tests.

If ascitic fluid cultures were positive and the neutrophil count was >250 cells/mm^3, patients were diagnosed as having culture- positive neutrocytic ascites or SBP. If ascitic fluid cultures were negative in the presence of neutrocytic ascites, patients were characterized as having culture negative neutrocytic ascites (CNNA).
Patients with positive cultures on ascitic fluid but without neutrocytic ascites were classified as having mono-bacterial bacterascites (MNB).

Ultrasound Scan
All patients underwent an abdominal ultrasound scan after overnight fasting and the following details were recorded: maximum vertical span of the liver; nodularity of liver surface; spleen size (length of its longest axis); and presence of ascites. The size of the kidneys and the presence or absence of corticomedullary differentiation were also determined. Enlarged abdominal lymph nodes and any other masses seen were also noted.

Other Investigations
A chest X- ray was performed for each patient, with clinical diagnoses of congestive heart failure and pneumonia as differentials. Features that were looked for included cardiomegaly, pulmonary oedema and areas of consolidation. Patients suspected of having abdominal tuberculosis also required a chest x-ray to exclude features suggestive of pulmonary tuberculosis.

Electrocardiography and Echocardiography were carried out for patients with a diagnosis of congestive heart failure for evidence of left ventricular hypertrophy and dilatation, atrial abnormalities, arrhythmias, and features of myocardial infarction, valvular lesions and other abnormalities. Abdominal CT scan was a further imaging investigation performed if the ultrasound scan was not sufficient enough to diagnose the cause of the ascites. Sputum for acid fast bacilli (AFB's,) Gene Xpert and adenosine deaminase of the ascitic fluid were further tests conducted on patients with clinical suspicion of abdominal tuberculosis.

Statistical Analysis
Data obtained were analyzed using the statistical package for social sciences (SPSS, version 18) statistical software. Descriptive statistics was undertaken for all the variables and data presented in appropriate graphs and tables. Causes of ascites and the prevalence of spontaneous bacteria peritonitis were determined. Further analysis was done to determine if there were any associations between spontaneous bacterial peritonitis and the clinical or laboratory parameters. Chi square was used to determine the level of association. A multivariate logistic regression analysis was conducted for clinical or laboratory parameters to determine if any of them were a

predictor of spontaneous bacterial peritonitis. A p-value less than 0.05 was considered significant.

Ethical Approval

The study conformed to the ethical guidelines of the University of Ghana Medical School and the Helsinki Declaration on Human Experimentation Sixth Revision (October 2008). A formal approval was obtained from the Ethical and Protocol Review Committee of the University of Ghana Medical School (Protocol Identification Number: CHS-Et/M.6 - P 3.2/2015-2016) The nature of the study was fully explained to potential participants. They were also informed that the study was entirely voluntary, and that non-participation would not jeopardize their immediate or subsequent medical care at the hospital. Participants who agreed to participate were asked to sign an informed consent form.

RESULTS

A total of 140 patients with ascites were recruited for the study with a mean age of 44.7±13.2 years (age range 18 to 74 years). Seventy-six (76) (54.3%) patients were males and 64 (45.7%) were females with male to female ratio of 1.1:1.

Ninety-nine (70.71%) of the patients had chronic liver disease (liver cirrhosis and hepatocellular carcinoma) as the cause of ascites, followed by malignancy excluding HCC (12.86%). Other causes of ascites included heart failure, nephrotic syndrome, chronic kidney disease, tuberculous ascites and unknown causes constituted 16.43%. (Figure 1)

SBP was present in 30 (21.43%) patients. Of the 30 patients that developed SBP, culture positive SBP was present in 26.67% (8/30) and CNNA was found in 63.33% (19/30). The prevalence of MNB was 10% (3/30) in this study. Among patients with the culture positive SBP, 5 (41.7%) positive cultures were due to E coli, followed by Corynebacterium spp. and Klebsiella spp. with 2 (16.7%) each. *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Streptococcus viridans* accounted for 1 (8.3%) of positive cultures (Table 1).

Majority of the participants with SBP were in relation to ascites caused by chronic liver disease (90.0%), with cancer induced ascites and heart failure ascites contributing only 6.6% and 3.3% respectively. No SBP was found in the other causes of ascites

Abdominal distension (100%), Weight loss (82.14%), pedal oedema (75.71%), abdominal pains (47.86%) and jaundice (42.86%) were the main clinical features. History of jaundice, low arterial blood pressure on admission and encephalopathy were found to be independent predictors of spontaneous bacterial peritonitis. (Table 2)

Laboratory parameters significantly predicting the presence of spontaneous bacterial peritonitis (SBP) were platelet count (OR = 1.01, p=0.017), INR (OR = 1.75, p=0.040), K^+ (OR = 0.27, p=0.026), fluid albumin (OR = 0.66, p=0.005). The overall model was also statistically significant (LR Chi2 = 64.74; p<0.0001) in predicting the presence of spontaneous bacterial peritonitis (SBP) (Table 3).

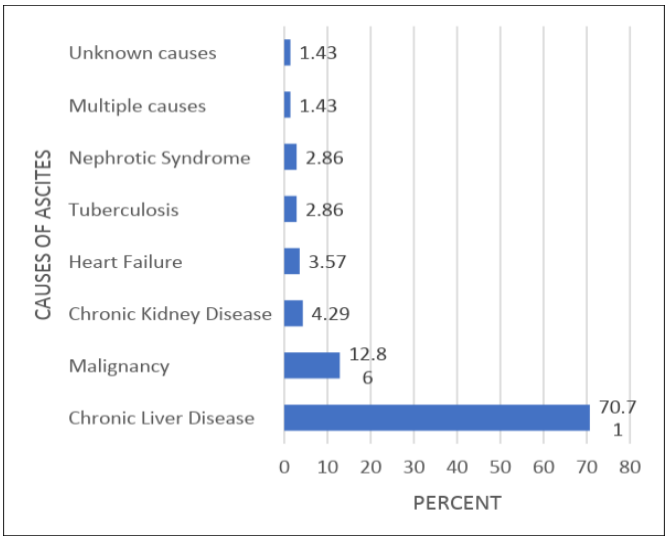

Figure 1 Aetiology of ascites

Table 2: Bacteria isolated from ascitic fluid

Organism	N (%)
Escherichia Coli	**5 (41.7)**
Corynebacterium spp	**2 (16.67)**
Klebsiella spp.	**2 (16.67)**
Staphylococcus aureus	**1 (8.33)**
Staphylococcus epidermidis	**1 (8.33)**
Streptococcus viridans	**1 (8.33)**
Total	**12 (100.0)**

Table: 3 Multiple Logistic regression model of independent risk factors (clinical features) of Spontaneous Bacterial Peritonitis.

Independent Risk factors	beta	Standard error	p-value	Adjusted Odds Ratio (AOR)	95% CI
Body Mass Index(Kg/m^2)	-0.1115	0.1091	0.307	0.8945	-0.3253 to 0.1023
Systolic BP(mmHg)	-0.1132	0.0381	0.003*	0.893	-0.1877 to -0.0386
Diastolic BP(mmHg)	-0.005	0.0538	0.925	0.995	-0.1104 to 0.1004

Independent Risk factors	**beta**	**Standard error**	**p-value**	**Adjusted Odds Ratio (AOR)**	**95% CI**
Ascites	-1.2058	0.9202	0.19	0.2994	-3.0094 to 0.5977
Jaundice	-2.0147	0.9633	0.036*	0.1334	-3.9028 to -0.1266
Abdominal pain	1.6158	0.8993	0.072	5.0318	-0.1469 to 3.3785
Fever	-16.9639	3884.545	0.997	4.29×10^{-8}	-7630.532 to 7596.604
Chills	18.8913	3884.545	0.996	1.60×10^{8}	-7594.676 to 7632.459
Weight loss	0.1065	1.0792	0.921	1.1124	-2.0087 to 2.2217
Pedal oedema	0.3366	1.23	0.784	1.4001	-2.0742 to 2.7474
Haematemesis	-0.9378	1.1349	0.409	0.3915	-3.1622 to 1.2866
Periorbital oedema	-1.2549	1.5884	0.43	0.2851	-4.3681 to 1.8584
Encephalopathy	2.3239	1.0536	0.027*	10.2153	0.2590 to 4.3888
Constant	15.8432	6.5834	0.016*	Not Applicable	2.9399 to 28.7465

Table 4 Multiple Logistic regression model of independent risk factors (laboratory parameters) of Spontaneous bacterial peritonitis.

Independent Risk factors	Odds Ratio (OR)	Standard error	p-value	95% CI
PLT. COUNT (10^9/L)	1.008	0.0034	0.017*	1.0014 to 1.0147
HB(g/l)	0.8054	0.1744	0.317	0.527 to 1.231
WBC (10^9/L)	0.9901	0.014	0.479	0.9631 to 1.0178
AST (U/L)	0.9966	0.0067	0.617	0.9835 to 1.0099
ALT (U/L)	0.9842	0.0182	0.389	0.9493 to 1.0205
SERUM ALBUMIN(g/l)	1.193	0.1134	0.063	0.9903 to 1.4372
TOT. PROTEIN(g/l)	0.9977	0.0358	0.949	0.9299 to 1.0704
TOT. BILIRUBIN (umol/l)	7.8796	12.0044	0.175	0.3978 to 156.0617
IND. BILIRUBIN (umol/l)	0.1298	0.1975	0.180	0.0066 to 2.56
DIR. BILIRUBIN (umol/l)	0.1267	0.1931	0.175	0.0064 to 2.5113
ALP (U/L)	1.0027	0.0032	0.403	0.9964 to 1.0089
GGT (U/L)	0.9968	0.0026	0.214	0.9917 to 1.0019
INR	1.7518	0.479	0.040*	1.0250 to 2.9937
Na^+(mmol/l)	0.9184	0.0498	0.116	0.8259 to 1.0213
K^+ (mmol/l)	0.2705	0.1592	0.026*	0.0853 to 0.8575
CREATININE (umol/l)	1.0036	0.0041	0.382	0.9956 to 1.0116
UREA (mmol/l)	0.8785	0.1078	0.291	0.6907 to 1.1174
FLUID ALBUMIN(g/l)	0.6565	0.0981	0.005*	0.4899 to 0.8799
F. TOTAL PROTEIN(g/l)	0.9993	0.0488	0.989	0.9082 to 1.0997

DISCUSSION

The mean age of the respondents was 44.7±13.20 years. This is worrying because this age bracket constitutes the working population. One must therefore consider the implications on economic productivity amongst these people and the burden it puts on society. This is similar to a study conducted in Côte d'Ivoire by Quattara et al.[26] which started the mean age of the participants as 44 ± 6 years but lower than a similar study done in Qatar with a mean age of 52.9 ± 14.8.[27] Similarities and differences in the mean age can be attributed to aetiologies of ascites and especially prevalence of hepatitis viruses in the population, as well as the timing of the spread of the viral infection. The age of individuals at the time of acquiring the infection is also important since cirrhosis was the most common cause in all the studies.

The prevalence of SBP among adult patients with ascites admitted at KBTH was 21.43%. Of the 30 patients that developed SBP, culture positive SBP was present in 26.67% (8/30) while CNNA was found in 63.33% (19/30). The prevalence of MNB was 10% (3/30) in this study. The prevalence of SBP in this study was lower compared with 67.7% reported by Oladimeji et al,[28] in Nigeria. This may be due to the fact that this study involved patients with ascites irrespective of the cause, whiles the study conducted by Oladimeji et al,[28] involved patients with only cirrhotic ascites in advance stage. SBP is more common in patients with ascites caused by cirrhosis in advanced stage. However, the results obtained are comparable to a prevalence of 21.2% reported by Such et al,[29] in 33 patients who had been hospitalized due to liver cirrhosis and Coşkun et al,[30] who reported a 20% SBP prevalence in 50 patients with cirrhosis.

Culture positive SBP reported by Oladimeji et al was 66.7%,[28] higher than this study while CNNA reported in this study was higher than one reported by the same study (33.3%). The prevalence of MNB in this study was 10%, similar to the 11% prevalence reported by Chu et al,[31] in Taiwan, but lower than 26% by Oladimeji et al.[28] The differences in prevalence could be explained by differences in culture methods and techniques used. Recent use of antibiotics may also contribute to the relatively low prevalence of culture positive SBP.

In this study E. coli (41.67%) was the most common organism isolated followed by Klebsiella species and Corynebacteria species each representing 16.67%. The rest of the organisms isolated were *Staphylococcus aureus* (8.33%), *Staphylococcus epidermidis* (8.33%) and *Streptococcus viridans* (8.33%).
The isolation of these organisms is consistent with studies done by Bhuva et al,[32] and Oladimeji et al,[28] which showed E. coli as the dominant bacteria cultured in patients with spontaneous bacterial peritonitis.

Majority of patients with SBP (90%) in this study were associated with ascites caused by chronic liver disease. This supports the report in literature that SBP associated with causes apart from ascites caused by chronic liver disease are rare enough to be the subject of case reports. The causes of ascites in this study apart from liver disease were few and that can also account for the predominance of SBP in ascites caused by chronic liver disease.The heterogeneity of the clinical and laboratory findings that is associated with the presence of SBP has been reported in various studies.

This justifies the indication for diagnostic paracentesis in all patients with ascites admitted in the hospital. Evan's et al,[33] did not identify any clinical or laboratory parameters to be associated with the presence of SBP whilst Figueiredo et al,[34] identified serum albumin, complement C4 of ascitic fluid and upper gastrointestinal bleeding as independent predictors for the diagnosis of SBP. Guarner et al,[35] also identified only serum bilirubin and platelet count as independent correlation with the presence of SBP. Hypoalbuminaemia, high model for end stage liver disease (MELD) score, C-reactive protein, encephalopathy and abdominal pains have also been reported by other studies to predict SBP.[36]

Low systolic blood pressure, jaundice, encephalopathy, platelet count and INR presented independent correlation with the development of SBP. Low blood pressure was found to have significant association with development of SBP. This can be the first manifestation of SBP or a complication of SBP. One of the recommendations for doing diagnostic paracentesis in cirrhotic patient with ascites is manifestation of hepatic encephalopathy. This is because infections including SBP are one of the main precipitant of encephalopathy.

The presence of jaundice in cirrhotic patient reflects the underlying deterioration of the liver condition or reflects bacteremia causing intravascular haemolysis. High INR, low platelet and low ascitic fluid albumin are consistent with advanced stage liver cirrhosis and SBP is high in patients with severe liver disease.[16,17] Fever and chills are common symptoms of infection and are also found in patients with SBP. In this study, fever at the time of presentation predicted SBP on univariate analysis but not multivariate analysis.

This study was not without limitations. The aetiology of ascites in this study was based mainly on clinical, laboratory and radiologic examinations. This method of diagnosis without any histologic basis may be less accurate as other causes of ascites could have been missed. Also, the mode of sampling had the potential of introducing selection bias; nevertheless, all patients who satisfied the inclusion criteria and did not have any of the exclusion criteria were selected.

CONCLUSION

Chronic liver disease was the common cause of ascites admitted at Korle-Bu Teaching. Spontaneous bacterial peritonitis was common among patients with ascites especially cirrhotic ascites admitted at Korle- Bu Teaching Hospital. Jaundice, encephalopathy, low blood pressure, high INR, low platelet and low ascitic fluid albumin were highly suggestive of spontaneous bacterial peritonitis and diagnostic paracentesis should be done immediately on admission to confirm the diagnosis preferably before starting empiric antibiotic therapy.

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